U.S. FOOD & DRUG ADMINISTRATION

May 16, 2022

Ally Danta
Senior Associate
Parexel International
Representing: Celltrion USA, Inc.
One Evertrust Plaza, Suite 1207
Jersey City, NJ 07302

Device:	Celltrion DiaTrust COVID-19 Ag Rapid Test
EUA Number:	EUA210190
Company:	Celltrion USA, Inc.
Indication:	Qualitative detection of SARS-CoV-2 nucleocapsid and receptor binding domain (RBD) antigens in direct mid-turbinate nasal swab specimens from individuals who are suspected of COVID-19 by their healthcare provider within the first 7 days of symptom onset, or from individuals without symptoms or other epidemiological reasons to suspect COVID-19 when tested twice over three days with at least 24 hours, and no more than 48 hours, between tests. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories:	Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high complexity, moderate complexity, or waived tests. This product is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Dear Ally Danta:

On April 16, 2021, based on your[1] request the Food and Drug Administration (FDA) issued Emergency Use Authorization (EUA) for the Celltrion DiaTrust COVID-19 Ag Rapid Test pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3) for the indications stated in the letter[2]. On May 11, 2021, FDA granted your

[1] For ease of reference, this letter will use the term "you" and related terms to refer to Celltrion USA, Inc.
[2] The April 16, 2021 letter authorized the Celltrion DiaTrust COVID-19 Ag Rapid Test for the qualitative detection of nucleocapsid and receptor binding domains (RBDs) from the SARS-CoV-2 in human nasopharyngeal swab

request to update to the authorized labeling.[3] Based on your request, the April 16, 2021, letter was revised and reissued by FDA on September 1, 2021.[4] On December 17, 2021, and March 9, 2022, FDA acknowledged your notices of additional distributors and minor changes to packaging and/or manufacturing processes.

On October 1, 2021, and January 31, 2022, FDA received requests from you to amend your EUA. In response to those requests, and having concluded that revising the September 1, 2021 EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), FDA is reissuing the September 1, 2021, letter in its entirety with the revisions incorporated[5] to authorize the emergency use of your product.[6] Pursuant to section 564 of the Act, Scope of Authorization (Section II) and Conditions of Authorization (Section III) of this reissued letter, your product is now intended for the indication above.

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19. Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of emergency use of in

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specimens directly collected from individuals who are suspected of COVID-19 by their healthcare provider within the first seven days of symptom onset, or from individuals without symptoms or other epidemiological reasons to suspect COVID-19 when tested twice over two or three days with at least 24 hours and no more than 48 hours between tests. Emergency use of this test is limited to authorized laboratories.

[3] On May 11, 2021, your request was granted via email to update the Instructions for Use (IFU) of the Celltrion DiaTrust COVID-19 Ag Rapid Test to fix some minor errors.

[4] On September 1, 2021, the revisions to the April 16, 2021, letter and authorized labeling included: (1) updates to expand the unopened shelf-life stability from 10 to 12 months when stored at 2-30°C; (2) updates to the Conditions of Authorization to add new conditions related to circulating SARS-CoV-2 variants (Conditions G. and H.) as well as E and F.; and (3) updates to the webpage links in the Fact Sheets for Healthcare Providers, and the date on the Fact Sheet for Patients was updated to match the date of re-issuance of the letter.

[5] The revisions to the September 1, 2021, letter and authorized labeling include: (1) updates to the intended use to remove nasopharyngeal specimens, add mid-turbinate nasal swab specimens and incorporate minor changes in wording to align with recent authorizations; (2) updates to expand the unopened shelf-life stability from 12 to 18 months when stored at 2-30°C; (3) addition of a condition of authorization for further evaluation of clinical performance of your test for detection of the SARS-CoV-2 omicron variant; (4) addition of conditions of authorization related to meeting the requirements of either ISO 13485 or 21 CFR 820 and removal of conditions of authorization related to meeting subparts of 21 CFR 820; (5) minor updates to the Fact Sheet for Patients and the Fact Sheet for Healthcare Providers to align wording with recent authorizations, match the date of reissuance of the letter, and update the webpage links in the Fact Sheets for Healthcare Providers; (6) updates to the IFU to: remove supporting data and instructions for use of nasopharyngeal specimens, add supporting data and instructions for use of mid-turbinate nasal swab specimens, add data from analytical testing of Omicron samples, align wording with recent authorizations, and match the date of re-issuance of the letter; (7) update the Conditions of Authorization Section to include "Authorized Distributors" and add some additional associated conditions of authorization, and add Condition L, (8) remove HUMASIS Co., Ltd. from the Conditions of Authorization section, and remove Waiver of Certain Requirements section (due to addition of condition L), and (9) minor updates to the Quick Reference Instruction (QRI) for clarity and to match the date of re-issuance of the letter.

[6] For ease of reference, this EUA will use the term "your product" to refer to the Celltrion DiaTrust COVID-19 Ag Rapid Test used for the indication identified above.

vitro diagnostics for detection and/or diagnosis of the virus that causes COVID-19 subject to the terms of any authorization issued under Section 564(a) of the Act.[7]

FDA considered the totality of scientific information available in authorizing the emergency use of your product for the indication above. A summary of the performance information FDA relied upon is included in the "Celltrion DiaTrust COVID-19 Ag Rapid Test Instructions for Use" (identified below).

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of your product, described in the Scope of Authorization of this letter (Section II), subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of your product meets the criteria for issuance of an authorization under Section 564(c) of the Act, because I have concluded that:

1. The SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that your product may be effective in diagnosing COVID-19, and that the known and potential benefits of your product when used for diagnosing COVID-19, outweigh the known and potential risks of your product; and

3. There is no adequate, approved, and available alternative to the emergency use of your product.[8]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited to the indication above.

Authorized Product Details

Your product is a lateral flow immunoassay intended for the qualitative detection of SARS-CoV-2 nucleocapsid and receptor binding domain (RBD) antigens in direct mid-turbinate nasal swab specimens from individuals who are suspected of COVID-19 by their healthcare provider within the first 7 days of symptom onset, or from individuals without symptoms or other epidemiological reasons to suspect COVID-19 when tested twice over three days with at least 24 hours, and no more than 48 hours, between tests. Your product does not differentiate between SARS-CoV and SARS-CoV-2.

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[7] U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*. 85 FR 7316 (February 7, 2020).

[8] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

The SARS-CoV-2 nucleocapsid and RBD protein antigen is generally detectable in human mid-turbinate nasal swab specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses.

Negative results should be treated as presumptive and confirmation with a molecular assay, if necessary, for patient management may be performed. Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19. For serial testing programs, additional confirmatory testing with a molecular test for negative results may be necessary, if there is a high likelihood of SARS-CoV-2 infection, such as in an individual with a close contact with COVID-19 or with suspected exposure to COVID-19 or in communities with high prevalence of infection. Additional confirmatory testing with a molecular test for positive results may also be necessary, if there is a low likelihood of SARS-CoV-2 infection, such as in individuals without known exposures to SARS-CoV-2 or residing in communities with low prevalence of infection.

Testing of mid-turbinate nasal swab specimens using your product, as outlined in the "Celltrion DiaTrust COVID-19 Ag Rapid Test Instructions for Use" is limited to laboratories certified under CLIA that meet the requirements to perform high complexity, moderate complexity, or waived tests. This product is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Your product is performed using mid-turbinate nasal swab samples. When using your product, the individual performing the test must follow instructions provided in the "Celltrion DiaTrust COVID-19 Ag Rapid Test Instructions for Use" or "Quick Reference Instruction Celltrion DiaTrust COVID-19 Ag Rapid Test" when collecting the specimen, running the test procedure and interpreting the results.

Your product requires various types of quality control, including the procedural internal control that is built in the 'control line (c)' of the test device and the external positive and negative controls, or other authorized control materials (as may be requested under Condition S. below), that are processed in the same way as the patient samples. All controls listed below must generate expected results in order for a test to be considered valid, as outlined in the Instructions for Use:

- Positive control swab – contains non-infectious recombinant SARS-CoV-2 RBD antigen and non-infectious recombinant SARS-CoV-2 nucleoprotein antigen dried onto the swab
- Negative control swab – sterile swab

Your product also requires the use of additional authorized materials and authorized ancillary reagents that are not included with your product and are described in the Instructions for Use.

The labeling entitled "Celltrion DiaTrust COVID-19 Ag Rapid Test Instructions for Use" and "Quick Reference Instruction Celltrion DiaTrust COVID-19 Ag Rapid Test" (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas), and the following fact sheets pertaining to the emergency use, are required to be made available as set forth in the Conditions of Authorization (Section III), and are collectively referred to as "authorized labeling":

- Fact Sheet for Healthcare Providers: Celltrion USA, Inc. - Celltrion DiaTrust COVID-19 Ag Rapid Test
- Fact Sheet for Patients: Celltrion USA, Inc. - Celltrion DiaTrust COVID-19 Ag Rapid Test

The above described product, when accompanied by the authorized labeling provided as set forth in the Conditions of Authorization (Section III), is authorized to be distributed to and used by authorized laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of your product, when used consistent with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of your product.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that your product may be effective in diagnosing COVID-19, when used consistent with the Scope of Authorization of this letter (Section II), pursuant to Section 564(c)(2)(A) of the Act.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that your product (as described in the Scope of Authorization of this letter (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of your product under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) of the Act described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1) of the Act, your product is authorized for the indication above.

III. Conditions of Authorization

Pursuant to Section 564(e) of the Act, I am establishing the following conditions on this authorization:

Celltrion USA, Inc. (You) and Authorized Distributor(s)[9]

A. Your product must comply with the following labeling requirements under FDA regulations: the intended use statement (21 CFR 809.10(a)(2), (b)(2)); adequate directions for use (21 CFR 809.10(b)(5), (7), and (8)); appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4); and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

B. You and authorized distributor(s) must make your product available with the authorized labeling to authorized laboratories.

C. You and authorized distributor(s) must make available on your website(s) the authorized labeling.

D. You and authorized distributor(s) must include a physical copy of the "Quick Reference Instruction Celltrion DiaTrust COVID-19 Ag Rapid Test" with each shipped product to authorized laboratories and must make the "Celltrion DiaTrust COVID-19 Ag Rapid Test Instructions for Use" electronically available with the opportunity to request a copy in paper form, and after such request, promptly provide the requested information without additional cost.

E. You and authorized distributor(s) must inform authorized laboratories and relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product and authorized labeling.

F. Through a process of inventory control, you and authorized distributor(s) must maintain records of the authorized laboratories to which they distribute your product and number distributed.

G. You and authorized distributor(s) must maintain customer complaint files on record. You must report to FDA any significant complaints about usability or deviations from the established performance characteristics of the product of which you become aware.

H. You and authorized distributor(s) must collect information on the performance of your product and have a process in place to track adverse events, including any occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the product of which you become aware and report any such events to FDA in accordance with 21 CFR Part 803. Serious adverse events, especially unexpected biosafety concerns, should immediately be reported to the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)-Office of In Vitro Diagnostics and Radiological Health (OIR)/Office of Product Evaluation and Quality

[9] "Authorized Distributor(s)" are identified by you, Celltrion USA, Inc., in your EUA submission as an entity allowed to distribute the Celltrion DiaTrust COVID-19 Ag Rapid Test.

(OPEQ)/Center for Devices and Radiological Health (CDRH) (via email: CDRH-EUAReporting@fda.hhs.gov).

I. You and authorized distributor(s) are authorized to make available additional information relating to the emergency use of your product that is consistent with, and does not exceed, the terms of this letter of authorization.

Celltrion USA, Inc. (You)

J. You must notify FDA of any authorized distributor(s) of your product, including the name, address, and phone number of any authorized distributor(s).

K. You must provide authorized distributor(s) with a copy of this EUA and communicate to authorized distributor(s) any subsequent revisions that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets).

L. Within three months of the date of this letter, you must establish and maintain a quality system that is appropriate for your product's design and manufacture, and that meets the requirements of either the 2016 edition of ISO 13485 or 21 CFR Part 820. You must submit to DMD/OHT7-OIR/OPEQ/CDRH a notification of compliance on such date.

M. If requested by FDA, you must submit associated documents or records related to your quality system for FDA review within 48 hours of the request.

N. You must have a signed agreement with each authorized distributor that ensures the distribution of the authorized product is consistent with this Letter of Authorization.

O. You must develop and implement a physical sampling procedure and final acceptance activities procedure within 2 weeks of the date of this letter. These procedures must be agreed to by DMD/OHT7-OIR/OPEQ/CDRH and include a process for sampling after importation and prior to distribution in the US. .

P. You must have lot release procedures and the lot release procedures, including the study design and statistical power, must ensure that the tests released for distribution have the clinical and analytical performance claimed in the authorized labeling.

Q. If requested by FDA, you must submit lot release procedures to FDA, including sampling protocols, testing protocols, and acceptance criteria, that you use to release lots of your product for distribution in the U.S. If such lot release procedures are requested by FDA, you must provide it within 48 hours of the request.

R. You must collect information on the performance of your product. You will report to DMD/OHT7-OIR/OPEQ/CDRH any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the product of which you become aware.

S. You may request changes to this EUA for your product, including to the Scope of Authorization (Section II in this letter) or to the authorized labeling, including requests to make available additional authorized labeling specific to an authorized distributor. Such additional labeling may use another name for the product but otherwise must be consistent with the authorized labeling and shall not exceed the terms of authorization of this letter. Any request for changes to this EUA should be submitted to DMD/OHT7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.

T. You must evaluate the analytical limit of detection and assess traceability[10] of your product with any FDA-recommended reference material(s). After submission to and review and concurrence with the data by FDA, you must update labeling to reflect the additional testing. Such labeling updates must be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

U. You must evaluate the clinical performance of your product to support the serial screening claim in an FDA agreed upon post authorization clinical evaluation study within 6 months of the date of this letter (unless otherwise agreed to with DMD/OHT7-OIR/OPEQ/CDRH). After submission to and concurrence with the data by FDA, you must update the authorized labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

V. You must further evaluate the clinical performance of your product for the detection of the SARS-CoV-2 omicron variant, in accordance with the FDA agreed upon post-authorization clinical evaluation study, within 4 months of the date of this letter (unless otherwise agreed to with DMD/OHT7-OIR/OPEQ/CDRH). After submission to and concurrence with the data by FDA, you must update the authorized labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

W. You must evaluate the impact of SARS-CoV-2 viral mutations on your product's performance. Such evaluations must occur on an ongoing basis and must include any additional data analysis that is requested by FDA in response to any performance concerns you or FDA identify during routine evaluation. Additionally, if requested by FDA, you must submit records of these evaluations for FDA review within 48 hours of the request. If your evaluation identifies viral mutations that affect the stated expected performance of your device, you must notify FDA immediately.

X. If requested by FDA, you must update your labeling within 7 calendar days to include any additional labeling risk mitigations identified by FDA, such as those related to the impact of viral mutations on test performance. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

[10] Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

Y. You must have a process in place to track adverse events, including any occurrence of false results and report to FDA pursuant to 21 CFR Part 803.

Authorized Laboratories

Z. Authorized laboratories using your product must include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating this labeling may be used, which may include mass media.

AA. Authorized laboratories using your product must use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including authorized instruments, authorized clinical specimen types, authorized control materials, authorized ancillary reagents and authorized materials required to use your product are not permitted.

BB. Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.

CC. Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

DD. Authorized laboratories must collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov), and Celltrion USA, Inc. (via email: Diatrust@celltrion.com or via phone: (201) 499-1844) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.

EE. All operators using your product must be appropriately trained in performing and interpreting the results of your product, use appropriate personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.

Celltrion USA, Inc. (You), Authorized Distributor(s) and Authorized Laboratories

FF. You, authorized distributor(s), and authorized laboratories using your product must ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

Conditions Related to Printed Materials, Advertising and Promotion

GG. All descriptive printed matter, advertising, and promotional materials relating to the use of your product shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and meet the requirements set forth in section 502(a), (q)(1), and (r) of the Act, as applicable, and FDA implementing regulations.

HH. No descriptive printed matter, advertising, or promotional materials relating to the use of your product may represent or suggest that this test is safe or effective for the detection of

SARS-CoV-2.

II. All descriptive printed matter, advertising, and promotional materials relating to the use of your product shall clearly and conspicuously state that:

- This product has not been FDA cleared or approved, but has been authorized by FDA under an EUA for use by authorized laboratories;
- This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens; and,
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

The emergency use of your product as described in this letter of authorization must comply with the conditions and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

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Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration

Enclosure

cc: KeeEun Lee, PhD, Team Leader, Global Regulatory Affairs Team
Bomin Kim, Team Leader, Global Regulatory Affairs Team
Celltrion USA, Inc.
One Evertrust Plaza, Suite 1207
Jersey City, NJ 07302